Suppression of lung growth by environmental toxins

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It is not unreasonable to expect that all children achieve their full lung growth potential. An important dimension of children's lung growth is growth of lung function. Over the last decade, long-term prospective studies have revealed that environmental toxins are an important threat to children's lung function growth. For example, the Southern California Children's Health Study found lower lung function growth in children living in communities with high background concentrations of fossil-fuel-derived particulate matter and nitrogen dioxide.[1] The cumulative effect of small annual deficits in lung function growth in highly polluted communities is an increased proportion of young adults with clinically low lung function (<80% predicted)[1]—a deficit that increases the risk of respiratory symptoms in adult life. The high prevalence of air pollution therefore means that most children growing up in medium-income and high-income countries will fail to achieve their maximum lung function growth potential. The difficulty of measuring FEV_1, and FVC from birth to 6 years of age means that it is unclear whether environmental insults in the first years of life disproportionately affect lung function growth. But there is increasing concern that exposures in early life fix an abnormal trajectory of lung growth that lasts throughout childhood.[2] A further barrier to teasing out the independent effect of exposures in early life on lung function growth is the high intercorrelation between exposure of pregnant women to air pollution and exposure of their children. However, early-life effects have recently been reported in studies where lung function has been measured at the absolute lower age limit for spirometry. For example, a recent analysis of the Infancia y Medio Amiente (INMA) cohort found that fetal exposure to benzene (an marker of fossil-fuel-derived pollution) during the second trimester is associated with clinically low lung function (<80% predicted, relative risk 1.2 (95% CI 1.02 to 1.46) at 4.5 years.[3] This strong evidence that air pollution attenuates lung function growth throughout childhood should stimulate studies into the effects of other environmental toxins—including the organophosphate (OP) pesticides. Most studies of the health effects of OP focus on exposure of adults in agricultural settings, and report a wide range of associations including increased prevalence of wheeze and lower lung function. More worrying is that effects of OP have also been observed in more general populations. For example, a recent analysis of the Canadian Health Measures Survey found an inverse association between total urinary dialkyl phosphate (DAP) concentrations (the major urinary metabolite of OP) and lung function in Canadian adults.[4] The study in this month's issue of Thorax by Raanan *et al*[5] of OP exposure in early life and lung function is therefore of significant interest. Using prenatal and postnatal urinary DAP concentrations from 279 Californian children in the Center for Health Assessment of Mothers and Children of Salinas (CHAMACOS), these researchers found an inverse association between early childhood urinary DAB and FEV_1 at 7 years of age, with no association between prenatal OP exposure and 7 year lung function. Whether the deficit in lung function associated with OP expsoure is fixed by the first year of life, or is from a small cumulative deviation in growth over 7 years remains unclear. Indeed, it may never be possible to obtain direct evidence of adverse effects of environmental toxins on lung function growth in the first years of life using spirometry variables that can be measured across the whole of childhood. However, further insights would be provided by prospectively tracking lung function growth in the CHAMACOS children. Follow-up may reveal both the pattern of lung function growth suppression during mid-childhood and late childhood, and indicate the possibility of recovery when OP exposure is reduced (reassuringly, the Southern California study found recovery of lung function growth when children moved out of highly polluted communities[6]). To date, there is no mechanism to explain why OP impairs lung function growth, although structural effects of OP have been reported in animal models. For example, OP induces airway hyperactivity via loss of neuronal M2 muscarinic receptor function.[7] What is needed now is not more animal studies with little relevance to lung function growth, but replication of Raanan *et al's*[5] data in another paediatric cohort. With creative thinking, it may be possible to perform spirometry in subjects where urinary DAP has already been assessed. For example, urinary DAP was detected in 63% children aged 6–11 years in the 2000 US National Health and Nutrition Examination Survey (NHANES) survey.[8] Since these NHANES children have now grown up, it may now be feasible to explore the link between childhood exposure to OP and adult lung function. In conclusion, the emerging link between exposure to environmental toxins and attenuated lung growth should remind policy makers to legislate for an environment in which all children are allowed to achieve their maximal lung function growth potential.

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